Roseane Gouveia [6], Fernando Domingues [7], Luciana Antunes [3], Valeria Oliveira [3]. [1] Instituto de Oncologia Pediátrica, São Paulo, Brazil; [2] Bone Marrow Transplantation, Instituto de Oncologia Pediátrica - GRAACC - Unifesp, São Paulo, Brazil; [3] Instituto de Oncologia Pediátrica - GRAACC - Unifesp; [4] Associação da Medula Óssea - AMEO; [5] Cell Processing Laboratory, Instituto de Oncologia Pediátrica, São Paulo, Brazil; [6] Transplante de Medula Óssea, Instituto de Oncologia Pediatrica, São Paulo, SP, Brazil; [7] Instituto de ONcologia Pediátrica - GRAACC - Unifesp

Allogeneic unrelated hematopoietic stem cell transplants (HSCT) are complex procedures that need adequate hospital infrastructure, a competent team, high-cost procedures and medications. Most transplants that are performed in Brazil are paid by the government. The national health system reimburses the hospital U$ 35,801.00 as a flat rate. The government has recently increased this amount by 60% but there are not national studies to use to evaluate the appropriateness of this amount. The objective of this study was to retrospectively evaluate the cost of ten consecutive unrelated donor HSCT performed in our institution.

Methods: The project was approved by our IRB (CEP-UNIFESP #1875/11) and granted waiver to request consent. The costs were evaluated from the first appointment until one year after transplant or death divided as 1) pre-HSCT, 2) conditioning therapy, 3) from the day of transplant until first discharge, 4) until D+100, 5) until D+180, and 6) until D+360. The costs included medications, supplies, blood transfusions, laboratory, imaging and the cost of the ward. Housing and out-of pocket costs or loss of income were not evaluated. Patients were scored 1 to 3 according to the Pediatric EBMT score.

Results: Ten consecutive children 2-14 years of age underwent unrelated donor HSCT from June, 2010 to May, 2011. Diagnoses were ALL (4). AML (3), lymphoma (2), and aplastic anemia (1). Three patients had early disease and others were in advanced phases of the disease. Eight were CMV positive. Five had marrow and five cord blood transplants. The median interval to transplant was 3.7 years from diagnosis and 80 days from referral. The patients remained hospitalized for a median of 80 days (21-50). Median time to engraftment was D+22 (12-56) and six had complications and needed Intensive Care support. Of the 10 children, seven were discharged but three eventually relapsed and died, overall survival is 50%. The median total cost during the first year was U$118,908.00 (mean U$ 139,861.00) − 44% of that spent within the first 100 days post HSCT. The first admission had a median total cost of U$ 64,385.00 (14,400 − 166,792). Total costs were approximately 40% higher than the direct cost. The highest costs were blood products and medications. No relationship was found between cost and age, gender, graft source of Pediatric EBMT-score.

Conclusion: Unrelated-donor HSCT is an expensive procedure and the government only partially reimburses its cost. Even with a 60% increase in reimbursement there will be a deficit in more than half of the procedures. We are working to increase the amount paid for specific complications and will have to continue to find alternative resources to pay for the transplants.

343

Allogeneic Hematopoietic Stem Cell Transplant in Patients Older Than 50 Years. Experience of Four Argentinean Centers

Mariano Berro [1], Viviana Montes de Oca [1], Maria Rivas [1], Ana Lisa Basquiera [2], Gregario Jaimovich [3], Juliana Martinez Rolon [4], Alejandro Requejo [5], Juan Garcia [6], Gustavo Kusminsky [1]. [1] Hematologia, Hospital Universitario Austral, Argentina; [2] Hospital Privado de Cordoba, Cordoba, Argentina; [3] Hematology, Fundacion Favaloro; [4] Transplant, Fundaleu, Buenos Aires, OS, Argentina; [5] Hematologia, Fundacion Favaloro; [6] Servicio de Hematologia y Oncologia, Hospital Privado de Cordoba, Cordoba, Argentina

Materials and Methods: We retrospectively reviewed 76 medical records of patients older than 50 years receiving an allogeneic HSCT in our centers. We evaluated the following characteristics: sex, age, diagnosis, stage, comorbidities (according to the HCT-CI score), type of donor, histocompatibility, conditioning and immunosupression. We analyzed the incidence and severity of Graft-vs-Host disease (GVHD) and treatment related mortality (TRM) with Chi Square and Overall Survival (OS) and Disease Free Survival (DFS) with Kaplan Meier. For multivariate analysis (MA) we used Cox regression model for time dependant outcomes and logistic regression for dichotomic variables, considering significant a $P < .05$.

Results: Between March 1998 and June 2012, 76 transplants were performed with a median follow up of 1.9 years. Fourteen patients were older than 60 years, 51 were male, HCT-CI score was 0 (41%), 1 (36%), ≥2 (23%), common diagnosis were AML (35%), MDS (30%) and MPN (20%), 65% were in late stage, 80% received a transplant from a MRD, 37% received FluMel conditioning regimen, 32% FluBu and 12% BuCy, 66% received tacrolimus (Fk) based regimen and 34% cyclosporine. Acute GVHD (aGVHD) incidence was 51%, aGVH grade II-IV 29%. AML patients had a lower incidence of aGVHD (36% vs. 61%, $P < .03$) still significant in MA (HR 0.27; 95% CI 0.07-0.98;$P = .04$) as well as FluMel conditioning (33% vs. 59%,$P = .02$), in contrast to unrelated donor (URD) (aGVHD GII-IV 53% vs. 23%,$P = .02$). Chronic GVHD incidence was 33%, extensive in 10%. Early TRM (day 100) was 17% and global 30%. Female patients had lower early TRM (4% vs. 25%,$P = .02$) opposite to HCT-CI score ≥2 patients that experienced a higher global TRM (58% vs. 26%, $P < .04$) still significant in MA (HR 4.6; 95% CI 1.03-20.9;$P = .04$) as well as MPN patients (64% vs. 25%, $P < .01$) also significant in MA (HR 7.2; 95% CI 1.20-43.7;$P = .03$). OS was 43% (1 year) and 20% (3 years). Patients older than 60 had a higher OS (1/3 years 61/43% vs. 38/14%;$P = .01$), while FluBu was associated to a lower OS (1/3 years 25/10% vs. 49/23%, $P < .05$), not significant in MA. Regarding immunosuppressant, the use of Fk was associated with a higher OS (1/3 years 44/20% vs. 19/6%, $P < .01$) significant in MA (HR 0.45; 95% CI 0.2-0.9;$P = .04$) and DFS (1/3 years 33/18% vs. 11/5%,$P = .01$).

Conclusion: According to the literature, URD is associated with a higher incidence of clinical significant aGVHD ($P = .02$) and FluMel presented lower incidence of aGVHD as well as AML patients. Regarding TRM female patients had a lower early TRM and lower HCT-CI score had lower global TRM. FluBu was associated with a lower OS, while Fk patients had a higher OS and DFS. Interestingly patients older than 60 had higher OS not significant in MA, probably due to a better selection: none had HCT-CI higher than 1, only 1 patient received an URD transplant, most of them received Fk base immunosuppressant and all of them received a NMA transplant.

344

Sequence-Based Discovery of Novel Bacteria, Bradyrhizobium Enterica, in Cord Colitis Syndrome

Ami S. Bhatt [1,2], Sam Freeman [2], Alex Herrera [1], Chandra Sekhar Pedamallu [1], Dirk Gevers [2], Joonil Jung [2], Fujiko Duke [2], Sarah Young [2], Ashlee Earl [2], Aleksandar Kostic [1,2],

Akinyemi Ojesina [1,2], Gabriela Soriano [3], Bruce J. Walker [2], Robert J. Soiffer [4], Joseph H. Antin [5], Lindsey Baden [6], Jason Hornick [7], Francisco Marty [4], Matthew Meyerson [1,2]. [1] Dana-Farber Cancer Institute; [2] Broad Institute; [3] Memorial Sloan-Kettering Cancer Center; [4] Dana-Farber Cancer Institute, Boston, MA; [5] Hematologic Malignancies, Dana-Farber Cancer Institute, Boston, MA; [6] Brigham and Women's Hospital, Boston, MA; [7] Brigham and Women's Hospital

Innate and therapy-induced states of immunosuppression are associated with a variety of potentially infectious idiopathic clinical syndromes. Using unbiased, next-generation sequencing, we investigated the metagenome of cord colitis syndrome (CCS), a recently described transplantation-associated colitis syndrome, in order to identify a candidate infectious trigger. Shotgun whole genome sequencing of DNA was performed followed by computational classification of reads. A large proportion of reads remained unmapped, suggesting the presence of a potentially novel organism. In order to investigate the source of these unmapped reads, *de novo* computational assembly of nonhuman reads was performed and yielded 98 contigs of $>$ 2.5kb in length covering a total of 7.65Mb. Read coverage and GC content was similar for all of these contigs, suggesting they corresponded to a common organism. Phylogenetic analysis of this draft genome revealed that this organism was a novel species, which we have provisionally named *Bradyrhizobium enterica*. PCR confirmed the presence of B. enterica in three additional CCS patients and demonstrated absence of B. enterica in normal colon, colon cancer and graft-versus-host disease controls. In summary, we have demonstrated the assembly of a novel bacterial draft genome from human tissue specimens without isolation or culture of the organism. This organism, provisionally named B. enterica, is associated with CCS suggesting that it may function as an opportunistic human pathogen.

345

An Identical Reduced Intensity Conditioning (RIC) Regimen Prior to Allogeneic (ALLO) Hematopoietic Stem Cell Transplantation (HSCT) in 222 Patients with Hematologic Malignancies: A Monocenter Experience

Didier Blaise [1], Luca Castagna [2], Geoffroy Venton [3], Roberto Crocchiolo [3], Jean EL-Cheikh [3], Sabine Furst [4], Claire Oudin [5], Angela Granata [3], Norbert Vey [6], Réda Bouabdallah [6], Christian Chabannon [7]. [1] Bone Marrow Transplant Unit, Institut Paoli Calmettes, Marseille, Cedex 9, France; [2] Unité de Greffe, Institut Paoli-Calmettes, Marseille, France; [3] Unité de Greffe, Institut Paoli-Calmettes, Marseille, France; [4] Institut Paoli Calmettes; [5] Institut Paoli-Calmettes; [6] Hematologie, Institut Paoli-Calmettes, Marseille, France; [7] Transplant and Cellular Therapy Unit, Institut Paoli Calmettes, Marseille, Cedex 9, France

Introduction: We have treated 222 consecutive patients eligible for allo HSCT with the same RIC from June 2005 up to March 2012. We particularly studied the impact of age, donor source and of the recent disease risk index (DRI) published by Amand et al (Blood 2012).

Patients and methods: All patients were treated for hematologic malignancies and were prepared with Fludarabin (30 mg/m^2/D x 5 D, IV Busulfan (3.2 mg/Kg/D x 2 D, and rabbit antithymocyte globulin (rATG) (2.5 mg/Kg/D x 2 D). All patients received CSA from D-1 with the addition of MMF in case of MMUD as post graft immunosuppression.

Table 1

*	Total
N	222
Age	58 (20-72)
HCT-SCI 0-1/2/>3	53/54/90
PS 90-100/70-80/50-60	107/108/7
AML/ALL/MDS/NHL and HD/MM/others	76/10/22/71/35/8
Disease Risk index Low/Int/High/VHigh	26/132/58/6 12%/59%/26%/3%
MRD/MUD/ MMUD	111/77/34 50%/35%/15%

* HCT-SCI indicates: hematopoietic cell transplantation specific comorbidity index; MRD, Matched related donor; MUD, Matched unrelated donor; MMUD, Mismatched unrelated donor

Table 2

	n	2-y OS	2-y PFS	2-y RR	2-y NRM
All patients	222	64%	54%	28%	20%
Low DRI	26 (12%	92%	69%	8%	13%
Int DRI	132 (59%)	69%	56%	27%	21%
High/VHigh DRI	64 (29%)	43%	40%	38%	31%
$>$ 58 years	120	61%	50%	/	27%
$<$ 58 years	102	67%	60%	/	16%
MRD	111	67%	53%	/	16%
MUD+ MMUD	111	60%	55%	/	28%

Results: As for August 2012, follow-up is 24 months (4-77). Patients characteristics are presented in Table 1; median age was 58 years with 45% and 30% of the patients presenting with a HCT-SCI $>$ 2 and a high or very high DRI respectively. 50% of donors were related siblings. Analyses of outcomes are presented in Table 2. Age only influenced NRM (P = .21). Donor origin has no influence on any outcome variable. DRI influenced OS (P = .000017) (Figure 1), PFS (P = .00045) (Figure 2), relapse (P = .0073) and at a lesser degree NRM (P = .056).

Conclusions: Overall results are promising. They validate the previously published DRI and indicate populations where efforts should be focused. Interestingly results are similar whatever the donor is.

346

Post-Transplant Outcome in Patients with Acute Myeloid Leukemia and Myelodysplasic Syndrome Who Received Conditioning Regimen Based on Fludarabin, Busulfan and Anti-Thymoglobulin Prior to Allogeneic Hematopoietic Stem Cell Transplantation

Didier Blaise [1], Claire Oudin [2], Patrice Chevallier [3], Sabine Furst [4], Thierry Guillaume [5], Jean EL-Cheikh [2], Roberto Crocchiolo [2], J. Delaunay [6], Anne Etienne [7], Norbert Vey [7], Mohamad Mohty [8]. [1] Bone Marrow Transplant Unit, Institut Paoli Calmettes, Marseille, Cedex 9, France; [2] Unité de Greffe, Institut Paoli-Calmettes, Marseille, France; [3] Hematologie, CHU NANTES, Nantes, France; [4] Institut Paoli Calmettes; [5] University of Louvain, Brussels, Belgium; [6] Institut Paoli-Calmettes; [7] Hematologie, Institut Paoli-Calmettes, Marseille, France; [8] Hematology Dpt, CHU de Nantes-Hotel-Dieu, Nantes, France

Purpose: Over the years, we have tuned the chemotherapy dose intensity of a busulfan based RIC regimen with the aim to better control disease while retaining a low toxicity profile. Here, we retrospectively analyzed a cohort of patients with myeloid malignancies treated identically in two French centers.

Patients and methods: From 2005 to 2010 in Marseille and Nantes we transplanted 165 patients (median age: 56.8 years